

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 04 MAY 2006

Applicant's or agent's file reference P2011PC00	FOR FURTHER ACTION	WIPO See Form PCT/IPEA/409	PCT
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International application No. PCT/DK2005/000027	International filing date (day/month/year) 17.01.2005	Priority date (day/month/year) 16.01.2004
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International Patent Classification (IPC) or national classification and IPC INV. G01N21/78 G01N21/25 G01N21/27 G01N33/04
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Applicant CHR. HANSEN A/S et al.

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
 - a. (*sent to the applicant and to the International Bureau*) a total of 5 sheets, as follows:
 - sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - b. (*sent to the International Bureau only*) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:
<input checked="" type="checkbox"/> Box No. I Basis of the report <input type="checkbox"/> Box No. II Priority <input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application

Date of submission of the demand 16.11.2005	Date of completion of this report 02.05.2006
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 TX: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Verdoodt, E Telephone No. +31 70 340-3577



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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
 - This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
 - international search (under Rules 12.3 and 23.1(b))
 - publication of the international application (under Rule 12.4)
 - international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

Description, Pages

1-24 as originally filed

Claims, Numbers

43-45 as originally filed
1-42 filed with telefax on 19.12.2005

Drawings, Sheets

1/14-14/14 as originally filed

a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. The amendments have resulted in the cancellation of:
 - the description, pages
 - the claims, Nos.
 - the drawings, sheets/figs
 - the sequence listing (*specify*):
 - any table(s) related to sequence listing (*specify*):
4. This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
 - the description, pages
 - the claims, Nos.
 - the drawings, sheets/figs
 - the sequence listing (*specify*):
 - any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
 - the entire international application,
 - claims Nos. 16,21-23,27
 - because:
 - the said international application, or the said claims Nos. 16,21-23,27 relate to the following subject matter which does not require an international preliminary examination (specify):
see separate sheet
 - the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 - the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 - no international search report has been established for the said claims Nos.
 - the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form has not been furnished
 does not comply with the standard
 - the computer readable form has not been furnished
 does not comply with the standard
 - the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- See separate sheet for further details

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-15,17-20,24-26,28-38
	No:	Claims	39-42
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-15,17-20,24-26,28-38,39-42
Industrial applicability (IA)	Yes:	Claims	1-15,17-20,24-26,28-38,39-42
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

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Re Item III.

- 1.1 **Claims 16, 21-23 and 27** relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(v) PCT.
- 1.2 Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V.

- 2 Reference is made to the following documents:
D1 : EP 0 301 699 A (UNIV UTAH) 1 February 1989
D2 : US 2001/039032 A1 (HYMAN JONES M ET AL) 8 November 2001

3 INDEPENDENT CLAIM 1

- 3.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject matter of claim 1 does not involve an inventive step in the sense of Article 33(3)PCT.
- 3.2 Document D1, which is considered to represent the most relevant state of the art to the subject matter of claim 1, discloses (the references in parentheses applying to this document):
A method for (...) determination of a biological, chemical or physical property of a plurality of individual samples of a turbid medium (Col. 1, lines 8-12) comprising the steps:
 - i) arranging said individual samples of the medium comprising a color indicator in an array (Col. 7, lines 8-11 and col. 11, lines 49-55);
 - ii) allowing said color indicator to interact with said samples (Col. 8, lines 24-27);
 - iii) *individually* examining said samples, following said interaction, using a *micro-colorimeter* (Figure 1 and Col. 15, lines 7-11) to determine the color developed on a surface of said sample (Col. 14, lines 21-35),
 - iv) to obtain a (...) value representation for said property, said (...) value representation being used for calculating a value for said property (Col. 12, lines 1-5).
- 3.3 The subject-matter of independent claim 1 differs from the disclosure of D1 in that the determination is performed *simultaneously* for a plurality of samples, as *picture capturing means* are provided for capturing a *digital image*, said digital image being used to obtain a digital value representation.
- 3.4 The technical effect can be seen as avoiding the need to position the colorimeter

exactly under each well, thus assuring that the same illumination conditions are achieved for every well at every measurement.

- 3.5 The problem to be solved by the present invention may therefore be regarded as how to ascertain equal illumination conditions for every sample, by preventing influence due to positional variations of the colorimeter.
- 3.6 In view of D2 the solution proposed in claim 1 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons: The feature to use picture capturing means for capturing a digital image (See paragraph 60: "CCD 2D array camera") being used to obtain a digital value representation (See figure 23, paragraph 171) is described in document D2 as providing the same advantages as in the present application. The skilled person would therefore regard it as a normal option to include this feature in the method described in document D1 in order to solve the problem posed.
- 3.7 Therefore the features disclosed in D1 and D2 would be combined by the skilled person, without exercise of any inventive skills in order to solve the problem posed. The proposed solution in independent claim 1 thus cannot be considered inventive (Article 33(3) PCT).

4 INDEPENDENT CLAIM 39

- 4.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 39 is not new in the sense of Article 33(2) PCT.
Document D2 discloses (the references in parentheses applying to this document):
A system (See figure 1) for determining a chemical or physical property of a turbid medium comprising:
 - i) a container (Figure 9; Paragraph 76: "Container for collecting sample") for containing a sample of said medium;
 - ii) an indicator (to be introduced: method step) in said sample, said indicator being adapted to indicate a specific value of said property by a specific color (Paragraphs 78, 79, 85 and 87);
 - iii) an incubator (206; see paragraph 42) for supporting said container and incubating said sample contained in said container;
 - iv) a scanner (208; see paragraphs 42 and 60) or digital camera for scanning said container, thereby generating an image file recording the color of said sample having reacted with the indicator;

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v) an analyser for analysing said image file and generating data values for image parameters for said image file and determining the value of said property of said sample from said image parameters (See paragraphs 61-72).

5 DEPENDENT CLAIMS 2-15, 17-20, 24-26, 28-38, 40-42

5.1 Dependent claims 2-15, 17-20, 24-26, 28-38, 40-42 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step (Article 33(2) and (3) PCT), in view of the passages of the documents cited in the Search Report.

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Claims

1. A method for simultaneous determination of a biological, chemical and/or physical property of a plurality of individual samples of a turbid medium comprising the steps:

- 5 i) arranging said individual samples of the medium comprising a color indicator in an array;
 ii) allowing said color indicator to interact with said samples;
 iii) providing picture capturing means for capturing a digital image of the color developed on a surface of said samples following said interaction;
 iv) using said digital image to obtain a digital value representation for said property, said
10 value representation being used for calculating a value for said property.

2. The method of claim 1 further comprising the step of comparing said digital value with the values obtained from a standardised set of samples having a range of known values representing said property to obtain a calculated value for said property.

- 15 3. The method according to claims 1 or 2, wherein said array is in the form of a container, such as a microtitre plate, having a plurality of wells arranged in an array format, said plurality being in the range of between 2 and 4000, such as 6, 24, 96, 384, or 1536 wells.

- 20 4. The method according to any one of claims 1 through 3, wherein said container has an transparent surface, such as a top or a bottom.

- 25 5. The method according to any one of claims 1 through 4, wherein said means for determination of color is a color-enabled photoelectric scanning device, that produces a digital color representation of said surface.

6. The method according to any one of claims 1 through 5, wherein said means is a scanning device.

- 30 7. The method according to any one of claims 1 through 6, wherein said scanning device is one of a line-by-line operating autofeed scanner, a flatbed scanner, a digital video camera and a digital camera.

- 35 8. The method according to any one of claims 1 through 7, wherein said scanning device operates on an at least partly open or transparent end of said container to generate an image file recording of the color of said sample.

9. The method according to claim 8, wherein said scanning device operates through the bottom of said container.

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10. The method according to any one of claims 1 through 9, wherein digital image processing methods are used to obtain an image file for determining the measuring positions from the digital color representation of said surface and for calculating said value for said property.

5 11. The method according to any one of claims 1 through 10 further comprising the step of illuminating the at least partly transparent surface of the container in connection with determining said color.

12. The method according to any one of claims 8 through 11, further comprising the steps:

- 10 i) analyzing said image file and generation of data values for image parameters by means of an analyzer; and
ii) translating said data values for image parameters to a value representing said chemical and/or physical property of said sample by means of said analyzer.

15 13. The method according to any one of claims 1 through 12, wherein said medium is liquid, semi-liquid or a gel.

14. The method according to any one of claims 1 through 13, wherein said medium is selected from the group consisting of biological fluids, such as dairy products, oil products, fruit juice products including jelly, spice products, beverages, whole blood, serum, or any combination thereof; as well as 20 emulsions including latex emulsions, mayonnaise, salad dressings, skin lotions and skin tonics.

15. The method according to any one of claims 1 through 14 wherein said medium contains live microorganisms, such as yeasts or lactic acid bacteria or both.

25 16. A method according to any one of claims 8 through 15, wherein said image file comprises an image format such as Synchronized Multimedia Integration Language (SMIL) format, any JPEG format, any Graphics Interchange Format (GIF), Computer Graphics Metafile, TIFF, BIFF, bmp, Clear, FITS, NFF, OFF, PCX, PNG, TGA, XBM, mod, Portable Document Format (PDF), Portable Network Graphics, Portable Pixmap, progressive coding, Quicktime, RIFF, Self Extracting Archive, sequential 30 coding, server-parsed HTML, sprite, Tagged Image File Format, targa, Targa Graphics Adaptor, thumbnail, wav, WebCGM, wireless bitmap, xpm or a different frame rate video or similar format.

17. A method according to claim 12, wherein said image parameters comprise lightness, chroma, Hue angle, or any combination thereof.

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18. A method according to claim 17, wherein said Hue angle determined from said image file is correlated with a pH level of said sample.

19. A method according to any one of claims 5 through 18, wherein said scanning of said container comprises scanning at predetermined intervals, preferably in the range from about 0.00001 second to about 60 to 120 minutes.

5 20. A method according to claim 12, wherein said analyzing of said image file is performed in predetermined regions of said container.

21. A method according to any one of claims 12 through 20 which further comprises saving said image parameters in a data file.

10 22. A method according to claim 21, wherein said data file is a comma-separated-value type file, a space-separated-value type file, a text type file, or any combinations thereof.

15 23. A method according to any one of claims 21 and 22 further comprising presenting said data file in graphical or textual form by means of a display.

24. A method according to any one of claims 12 through 23, wherein said analyzer comprises a digital processor such as in a computer, a server system, a personal digital assistant, a cell phone, or any combination thereof.

20 25. A method according to claim 24, wherein said analyzer further comprises a memory device for storing an analyzing program code to be executed by the processor, for storing image files recorded by the scanner, and for storing data values generated by the analyzer.

25 26. A method according to any one of claims 24 and 25, wherein said memory device and/or said scanner is adapted to connect to said processor through a computer network such as a dedicated line network, a local area network, a wide area network, a metropolitan area network, or an inter-network.

30 27. A method according to any one of claims 12 through 26, wherein said analyzer further comprises a display for displaying progress of said analyzing of said image file and/or displaying said data file such as a monitor for presenting textual or graphical data such as a personal computer monitor, personal digital assistant monitor, cell phone display, or any combination thereof.

35 28. The method according to any one of claims 1 through 27, wherein said property is the pH of the medium.

29. The method according to any one of claims 1 through 28, wherein said color indicator is a pH indicator.

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30. The method according to claim 29, wherein said pH indicator is adapted to indicate pH levels between 3 and 8, the indicators being preferably selected from the group consisting of bromocresol green, bromocresol purple, bromophenol blue, bromothymol blue, chlorophenol red, phenol red, etc.

5 31. The method according to any one of claims 1 through 30, wherein said medium is milk, a processed milk product, whey, and/or a bacteriological medium optionally comprising live lactic acid bacteria.

10 32. The method according to claim 31, which further comprises adding bacterial cultures to said sample in said array or container.

33. The method according to claim 31, wherein determination of pH is an indication of bacteriophage infection of the lactic acid bacteria.

15 34. The method according to any one of claims 1 through 27, wherein said property is the viscosity of the medium.

35. The method according to claim 34, wherein said medium is yogurt.

20 36. The method according to any one of claims 34 and 35 wherein said color indicator is brilliant blue or Ruthenium Red.

37. The method according to any one of claims 34 through 36, wherein said color indicator is added to the top surface of or into the sample after adding the sample to the container.

25 38. The method according to any one of claims 34 through 37, wherein said color indicator is allowed to interact with said sample according to a predetermined time wherein a development at the bottom of said sample surface is known to correspond to a specific viscosity of said medium.

30 39. A system for determining a chemical or physical property of a turbid medium comprising:

- I) a container for containing a sample of said medium;
- II) a indicator to be introduced in said sample said indicator being adapted to indicate a specific value of said property by a specific color;
- III) an incubator for supporting said container and incubating said sample contained in said container;
- IV) a scanner or digital camera for scanning said container thereby generating an image file recording the color of said sample having reacted with the indicator,
- V) an analyzer for analyzing said image file and generating data values for image parameters for said image file and determining the value of said property of said sample from said image parameters.

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40. The system of claim 39 wherein said property is the acidity of said medium as measured by pH and said indicator is a pH indicator.

5 41. The system of claim 39 wherein said property is the viscosity of said medium and said indicator is a colored substance characterised in having a time for penetration of said sample which is correlated with the viscosity of said sample.

10 42. A system according to any one of claims 39 through 41, wherein said system comprises any feature of the method according to any one of claims 1 through 38.